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PILLSBURY WINTHROP LLP
INTELLECTUAL PROPERTY GROUP
11682 EL CAMINO REAL, SUITE 200
SAN DIEGO, CA 92130-2593

EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	20

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/549,096	WARE, CARL	
	Examin r	Art Unit	
	" Neon" Phuong Huynh	1644	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/16/02; 9/17/02; 12/05/02* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-52* is/are pending in the application.

4a) Of the above claim(s) *1-25,33 and 37-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-32, 34-36 and 51-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 September 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-52 are pending.

2. Newly submitted claim 51 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claim 51 drawn to a method for inhibiting a p30 polypeptide-mediated cellular response comprising a composition that binds to a p30 polypeptide, HVEM or LTβR wherein the composition is antibody, or fusion protein, or functional fragment p30 polypeptide, HVEM or LTβR. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 51 drawn to the method wherein the composition is antibody is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Claim 51 that read on the fusion polypeptide and functional fragment p30 polypeptide, HVEM or LTβR will be examined along with the elected invention drawn to a method for inhibiting a p30 polypeptide-mediated cellular response using a composition comprising a polypeptide.

3. Claims 1-25, 33 and 37-50 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. The following new grounds of objection and rejection are necessitated by the amendment filed 9/16/02, 9/17/02 and 12/05/02.

5. The disclosure is objected to because of the following informality: the Brief Description of the Figures is no longer match the amended Figures submitted on September 17, 2002, for example, the Number and letter in Figure 1 indicates **FIG. 1A-1, FIG. 1A-2, FIG. 1B-1, Fig 1B-2, FIG. 1C** while the Brief Description of the Figures discloses **Figure 1A, Figure 1B, Figure 1C**. It is suggested that Applicant amended the Brief Description of the Figures to match the newly submitted Figures. Appropriate action is required.

6. Amended Claim 26 is objected to because a clean copy of the claim **without underline** and a copy of the claim to show changes made (with underline) are required. Appropriate action is required.

7. Claim 51 is objected to because it recites antibody, which drawn to a non-elected invention.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 26-32, 34-36 and 51-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) A method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response comprising a) providing a composition that binds to a p30 polypeptide, HVEM or LTβR and that inhibits binding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR, said p30 polypeptide having an apparent molecular weight of about 30 kDa as determined by SDS-PAGE and an isoelectric charge (pI) of between about pI 7 to about pI 8.5 and that binds HVEM or LTβR; and (b) contacting the cell expressing the cell surface expressed HVEM or LTβR with an amount of the composition sufficient to inhibit a p30 polypeptide-mediated cellular response wherein the composition comprises a soluble p30 polypeptide, (2) A method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response comprising a) providing a composition that binds to a p30 polypeptide, HVEM or LTβR and that inhibits binding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR, said p30 polypeptide having an apparent molecular weight of about 30 kDa as determined by SDS-PAGE and an isoelectric charge (pI) of between about pI 7 to about pI 8.5 and that binds HVEM or LTβR; and (b) contacting the cell expressing the cell surface expressed p30 polypeptide of SEQ ID NO: 6 with an amount of the composition sufficient to inhibit a p30 polypeptide-mediated cellular response wherein the composition comprises a soluble HVEM polypeptide, (3) the methods mentioned above wherein the cell is contacted with said composition in vivo, (4) the methods mentioned above wherein the inhibiting a p30 polypeptide mediated cellular response comprises inhibition of a lymphocyte cellular response such as lymphocyte proliferation, (5) the methods mentioned above wherein the inhibited lymphocyte is a pathologenic effector cell mediated inflammation (delayed-type

hypersensitivity) or collagen induced arthritis, and (6) the methods mentioned above wherein the composition that binds to a p30 polypeptide, HVEM or LTβR is selected from the group consisting of HSV gD-1, HVEM:Fc, LTβR:Fc or LIGHT-t66, **does not** reasonably provide enablement for (1) a method for inhibiting a p30 polypeptide-mediated cellular response comprising providing *any* "**composition**" that binds to a p30 polypeptide, HVEM or LT or LTβR and inhibits biding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR, said p30 polypeptide having an apparent molecular weight of about 30kDa as determined by SDS-PAGE and an isoelectric charge (pI) of between about pI 7 to about pI 8.5 and that binds HVEM or LTβR and (b) contacting the cell expressing the cell surface expressed p30 polypeptide or HVEM or LTβR with an amount of the "**composition**" sufficient to inhibit a p30 polypeptide-mediated cellular response, (2) the said method wherein the cells is contacted with any composition in vivo with any composition, (3) the said method wherein the inhibited p30 polypeptide-mediated response comprises inhibition of any lymphocyte cellular response with any composition, (4) the said method wherein the inhibited lymphocyte response is lymphocyte proliferation with any composition, (5) the said method wherein the inhibited lymphocyte response is any pathalogenic effector cell, (5) the said method wherein the inhibited lymphocyte response "modulates" a T or B lymphoma or leukemia or any autoimmune disease, (6) method for inhibiting a p30 polypeptide-mediated cellular response comprising providing *any* "**composition**" that binds to a p30 polypeptide, HVEM or LT or LTβR and inhibits biding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR, said p30 polypeptide having an apparent molecular weight of about 30kDa as determined by SDS-PAGE and an isoelectric charge (pI) of between about pI 7 to about pI 8.5 and that binds HVEM or LTβR and (b) contacting the cell expressing the cell surface expressed p30 polypeptide or HVEM or LTβR with an amount of the "**composition**" sufficient to inhibit a p30 polypeptide-mediated cellular response wherein the autoimmune disease is rheumatoid arthritis, insulin dependent diabetes mellitus, multiple sclerosis, systemic lupus erythematosus or myasthenia gravis, (7) method for inhibiting a p30 polypeptide-mediated cellular response comprising providing *any* "**composition**" that binds to a p30 polypeptide, HVEM or LT or LTβR and inhibits biding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR, said p30 polypeptide having an apparent molecular weight of about 30kDa as determined by SDS-PAGE and an isoelectric charge (pI) of between about pI 7 to about pI 8.5 and that binds HVEM or LTβR and (b) contacting the cell expressing the cell surface expressed p30 polypeptide or HVEM

or LTβR with an amount of the "**composition**" sufficient to inhibit a p30 polypeptide-mediated cellular response wherein the composition that binds to any p30 polypeptide, HVEM, or LTβR is any antibody, *any* fusion protein comprising *any* p30 polypeptide, HVEM, or LTβR, or any functional fragment of *any* p30 polypeptide, HVEM, or LTβR for inhibiting any p30 polypeptide mediated cellular response, or *any* gD-1 (290-299t). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only three compositions wherein the composition consisting of a soluble polypeptide selected from the group consisting of HSV gD-1 protein, LIGHT t66, and HVEM:Fc chimeric protein for a method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response comprising a) providing a HSV gD-1 protein that inhibits binding of a cell surface expressed HVEM ligand (also known as LIGHT t66), which is a soluble homotrimeric p30 polypeptide consisting of SEQ ID NO: 6 to a cell surface expressed HVEM *in vitro*, which is a receptor or lymphotoxin beta receptor (LTβR), and b) contacting the cell surface expressed p30 polypeptide of SEQ ID NO: 6 or the cell surface expressed HVEM or LTβR with an amount of the composition sufficient to inhibit a p30 polypeptide of SEQ ID NO: 6-mediated cellular response wherein said composition is soluble HSV gD-1 or mouse HVEM:Fc chimeric protein or LIGHT t66 (2) the said method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response wherein the cellular response is lymphocyte proliferation; (3) a method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated inflammation (delayed-type hypersensitivity) in vivo comprising providing a composition that inhibits the binding of p30 polypeptide of SEQ ID NO: 6 to the HVEM receptor wherein the composition is a soluble mouse HVEM:Fc chimeric protein; (4) a method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated collagen induced arthritis in vivo comprising providing a composition that inhibits the

binding of p30 polypeptide of SEQ ID NO: 6 to the HVEM receptor wherein the composition is a soluble mouse HVEM:Fc chimeric protein (page 56).

The specification does not teach how to make and use *any* **composition** for the claimed method of inhibiting any p30 polypeptide-mediated cellular response because there is insufficient guidance as to what is in the claimed composition, much less inhibiting a p30 polypeptide mediated cellular response, in turn, "modulates" lymphoma, leukemia or any autoimmune disease such as the ones recited in claim 32. Given the indefinite number of undisclosed composition, it is unpredictable which undisclosed composition is effective for the claimed method. Further, there is insufficient working example demonstrating that any composition would be effective for the claimed method of inhibiting any p30 polypeptide-mediated cellular response.

Even if the composition is limited to p30 polypeptide, the soluble p30 polypeptide as recited in claim 34 and 35, the p30 polypeptide is not necessary the same p30 polypeptide recited in claim 26. A p30 polypeptide without SEQ ID NO lacks structure much less about the function such as inhibiting a p30 polypeptide mediated cellular response. There is insufficient guidance as to the structure of p30 polypeptide such as the ones recited in claims 34-36 associated with function. There is insufficient working example demonstrating that any p30 polypeptide is effective for the claimed method, in turn, for modulating T or B cell lymphoma or treating any autoimmune disease. Given the indefinite number of p30 polypeptide, it is unpredictable which undisclosed p30 polypeptide is effective for the claimed method. Since the amino acid sequence of a polypeptide determines its structural and functional properties, in the absence of guidance as to the composition comprising the specific polypeptide, it would take undue amount of experimentation even for one skill in the art to practice the claimed invention. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe nor enable any composition other than the composition comprising the specific polypeptide such as the ones recited in claim 52 for a method for inhibiting a p30 polypeptide-mediated cellular response.

With regard to autoimmune disease such as the ones recited in claim 32, other than the specific composition comprising the specific polypeptide mentioned above for inhibiting lymphocyte proliferation, delayed-type sensitivity, and collagen induced arthritis as a model for rheumatoid arthritis, the specification fails to provide sufficient in vivo working examples and guidance for modulate T or B lymphoma or leukemia or any autoimmune disease such as rheumatoid arthritis, insulin dependent diabetes, multiple sclerosis, systemic lupus erythematosus

or myasthenia gravis because the word "modulate" can be inhibiting or stimulating. Further, in vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the method of treating and modulating autoimmune disease can be species- and model-dependent, it is not clear that reliance on the in vitro lymphocyte proliferation assay and one in vivo experimental model for collagen induced arthritis accurately reflects the efficacy of the claimed method of modulating T or B lymphoma, leukemia or any autoimmune disease comprising administering any composition comprising any p30 polypeptide.

Van Noort *et al,* of record, tech that animal models of autoimmune diseases varies with respect to genetics strains, MHC haplotpes, antigen used, immunization protocols, for example, induction of autoimmune disease such as EAE with MBP does not result in the development of relapses (See page 167-170, in particular). Tian *et al,* of record, teach that in experimentally induced organ specific autoimmune disease models, the initiating antigen is defined. However, an initiating target antigen has not yet defined in human T-cell mediated autoimmune disease such as MS or IDDM (See page 190, in particular). Tian *et al* further teach that animal models of T-cell-mediated autoimmune disease rely on specific MHC genotypes and the animals often genetically predisposed to developing polarized immune response, these are likely to contribute to their disease susceptibility as well as their amenability to immunotherapy. By contrast, human MHC types are highly polymorphic, and little is known about antigen processing and presentation in this context, as well as what factors determine the nature of the immune response and possible long-term treatment (See page 193, column 1, in particular). Since treating autoimmune disease can be species-and model-dependent, it is not clear that reliance on the collagen induced arthritis for rheumatoid arthritis using one specific HVEM:FC polypeptide accurately reflects the efficacy of the claimed method for treating other autoimmune diseases such as the ones mentioned above. Furthermore, the method of inhibiting a p30 polypeptide mediated cellular response using any composition other than the specific polypeptide in the absence of in vivo data is unpredictable for the following reasons: (1) the soluble polypeptide may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the polypeptide; (2) the polypeptide may not reach the target area because, i.e. the polypeptide may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the polypeptide unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment.

With regard to newly added claim 51, there is insufficient guidance about the structure of any "fusion protein" because it is not clear what is being fused to the p30 polypeptide or the HVEM or LTβR. The specification discloses only chimeric protein comprising p30 polypeptide or the HVEM or LTβR fused to the Fc region of an immunoglobulin. Further, there is insufficient working example that any fusion protein is effect for the claimed method which inhibits any p30 polypeptide-mediated cellular response, including modulates a T or B lymphoma or leukemia or any autoimmune disease. With regard to "functional fragment", there are insufficient guidance as to which fragment i.e. specific amino acids within the full length of the p30 polypeptide or the HVEM or LTβR is functional such as inhibits a p30 polypeptide-mediated cellular function, not to mentioned modulates a T or B lymphoma or leukemia or any autoimmune disease.

With regard to newly added claim 52, the recitations of HSV gD-1, gD-1 (Δ290-299t) or LIGHT-t66 without SEQ ID NO have no structure such as amino acid sequence associated with function because said HSV gD-1, gD-1 (Δ290-299t) or LIGHT-t66 are merely a laboratory designation which does not clearly define the polypeptide in the claimed method, since different laboratories may use the same laboratory designations define completely distinct polypeptides.

For these reasons, the specification as filed fails to enable one skill in the art to practice the invention as broadly as claimed without undue amount of experimentation. In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. As such, further research would be required. In view of the quantity of experimentation necessary, the insufficient number of working examples, the unpredictability of the art, the insufficient guidance and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

Applicants' arguments filed 9/16/02, 9/17/02 and 12/05/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) claim 26 has been amended such that the composition "binds to a p30 polypeptide, HVEM or LTβR and (2) the composition inhibits binding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR. (2) The specification teaches how to identify compositions having the recited function. (3) The specification exemplifies four different composition, soluble HSV gD-1, gD-1 (Δ290-299t), HVEM:Fc, LTβR:Fc, and LIGTH-t66. (4) the claims are not directed to treating any autoimmune disease. Rather, claim 26 is directed to inhibiting cellular response and lymphoma, leukemia and

autoimmune disease in depending claims 31 and 32 are mediated at least in part by a p30 polypeptide-mediated cellular response. The Van Noort et al reference do not suggest that cytokine based methods of autoimmune treatment will be unsuccessful. Tian et al reference is irrelevant to the claimed method.

In response to Applicant's argument to items 1-3, although the claim has been amended, claim 26 still recites a method of inhibiting any p30 polypeptide-mediated cellular response using any composition since a composition could be any polypeptide, DNA, antibody, or small molecule. It is not clear what is in the composition for the claimed method because there is no structure associated with the term "composition", let alone the claimed method of inhibiting any p30 polypeptide-mediated cellular response such as "modulates" a T or B lymphoma, or leukemia or any autoimmune disease such as the ones recited in claim 32. Given the indefinite number of undisclosed composition, it is unpredictable which undisclosed composition is effective for the claimed method. Further, there is insufficient working example demonstrating that any composition would be effective for the claimed method of inhibiting any p30 polypeptide-mediated cellular response. Even if the composition is limited to p30 polypeptide, the soluble p30 polypeptide as recited in claim 34 and 35, the p30 polypeptide is not necessary the same p30 polypeptide recited in claim 26. A p30 polypeptide without SEQ ID NO lacks structure much less about the function such as inhibiting a p30 polypeptide mediated cellular response. There is insufficient guidance as to the structure of p30 polypeptide such as the ones recited in claims 34-36 associated with function. There is insufficient working example demonstrating that any p30 polypeptide is effective for the claimed method, in turn, for modulating T or B cell lymphoma or treating any autoimmune disease. Given the indefinite number of p30 polypeptide, it is unpredictable which undisclosed p30 polypeptide is effective for the claimed method. Since the amino acid sequence of a polypeptide determines its structural and functional properties, in the absence of guidance as to the composition comprising the specific polypeptide, it would take undue amount of experimentation even for one skill in the art to practice the claimed invention. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. Other than the specific composition comprising the specific polypeptide such as the ones recited in claim 52 for a method for inhibiting a p30 polypeptide-mediated cellular response, the specification does not describe nor enable any composition for a method for inhibiting a p30 polypeptide-mediated cellular response.

In response to Applicant's argument to item 4, Claim 26 and 32 taken as a whole read on the method of treating any autoimmune disease such as "modulates a T or a B lymphoma, or leukemia, or any autoimmune disease. Further the word "modulates" can be inhibiting as well as stimulating and both actions are mutually exclusive. There is insufficient guidance as to which autoimmune disease, T or B lymphoma or leukemia that the claimed method stimulate or inhibit the p30 polypeptide mediated cellular response.

Van Noort *et al,* of record, tech that animal models of autoimmune diseases varies with respect to genetics strains, MHC haplotpes, antigen used, immunization protocols, for example, induction of autoimmune disease such as EAE with MBP does not result in the development of relapses (See page 167-170, in particular). Tian *et al,* of record, teach that in experimentally induced organ specific autoimmune disease models, the initiating antigen is defined. However, an initiating target antigen has not yet defined in human T-cell mediated autoimmune disease such as MS or IDDM (See page 190, in particular). Both references teach that treating autoimmune disease can be species-and model-dependent. It is not clear that reliance on the collagen induced arthritis for rheumatoid arthritis using one specific HVEM:FC polypeptide accurately reflects the efficacy of the claimed method for any other autoimmune diseases such as the ones recited in claim 32. Furthermore, the method of inhibiting a p30 polypeptide mediated cellular response using any composition other than the specific polypeptide in the absence of in vivo data is unpredictable for the following reasons: (1) the soluble polypeptide may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the polypeptide; (2) the polypeptide may not reach the target area because, i.e. the polypeptide may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the polypeptide unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment.

10. Claims 26-32, 34-36 and 51-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) a method for inhibiting a p30 polypeptide-mediated cellular response comprising providing *any* "**composition**"

that binds to a p30 polypeptide, HVEM or LT or LTβR and inhibits biding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR, said p30 polypeptide having an apparent molecular weight of about 30kDa as determined by SDS-PAGE and an isoelectric charge (pI) of between about pI 7 to about pI 8.5 and that binds HVEM or LTβR and (b) contacting the cell expressing the cell surface expressed p30 polypeptide or HVEM or LTβR with an amount of the "**composition**" sufficient to inhibit a p30 polypeptide-mediated cellular response, (2) the said method wherein the cells is contacted with any composition in vivo with any composition, (3) the said method wherein the inhibited p30 polypeptide-mediated response comprises inhibition of any lymphocyte cellular response with any composition, (4) the said method wherein the inhibited lymphocyte response is lymphocyte proliferation with any composition, (5) the said method wherein the inhibited lymphocyte response is any pathalogenic effector cell, (5) the said method wherein the inhibited lymphocyte response "modulates" a T or B lymphoma or leukemia or any autoimmune disease, (6) method for inhibiting a p30 polypeptide-mediated cellular response comprising providing *any* "**composition**" that binds to a p30 polypeptide, HVEM or LT or LTβR and inhibits biding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR, said p30 polypeptide having an apparent molecular weight of about 30kDa as determined by SDS-PAGE and an isoelectric charge (pI) of between about pI 7 to about pI 8.5 and that binds HVEM or LTβR and (b) contacting the cell expressing the cell surface expressed p30 polypeptide or HVEM or LTβR with an amount of the "**composition**" sufficient to inhibit a p30 polypeptide-mediated cellular response wherein the autoimmune disease is rheumatoid arthritis, insulin dependent diabetes mellitus, multiple sclerosis, systemic lupus erythematosus or myasthenia gravis, (7) method for inhibiting a p30 polypeptide-mediated cellular response comprising providing *any* "**composition**" that binds to a p30 polypeptide, HVEM or LT or LTβR and inhibits biding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR, said p30 polypeptide having an apparent molecular weight of about 30kDa as determined by SDS-PAGE and an isoelectric charge (pI) of between about pI 7 to about pI 8.5 and that binds HVEM or LTβR and (b) contacting the cell expressing the cell surface expressed p30 polypeptide or HVEM or LTβR with an amount of the "**composition**" sufficient to inhibit a p30 polypeptide-mediated cellular response wherein the composition that binds to any p30 polypeptide, HVEM, or LTβR is any antibody, *any* fusion protein "**comprising**" *any* p30 polypeptide, HVEM, or LTβR, or any functional fragment of *any*

p30 polypeptide, HVEM, or LTβR for inhibiting any p30 polypeptide mediated cellular response, or *any* gD-1 (290-299t).

The specification discloses only three compositions wherein the composition consisting of a soluble polypeptide selected from the group consisting of HSV gD-1 protein, LIGHT t66, and HVEM:Fc chimeric protein for a method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response comprising a) providing a HSV gD-1 protein that inhibits binding of a cell surface expressed HVEM ligand (also known as LIGHT t66), which is a soluble homotrimeric p30 polypeptide consisting of SEQ ID NO: 6 to a cell surface expressed HVEM in vitro, which is a receptor or lymphotoxin beta receptor (LTβR), and b) contacting the cell surface expressed p30 polypeptide of SEQ ID NO: 6 or the cell surface expressed HVEM or LTβR with an amount of the composition sufficient to inhibit a p30 polypeptide of SEQ ID NO: 6-mediated cellular response wherein said composition is soluble HSV gD-1 or mouse HVEM:Fc chimeric protein or LIGHT t66 (2) the said method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated cellular response wherein the cellular response is lymphocyte proliferation; (3) a method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated inflammation (delayed-type hypersensitivity) *in vivo* comprising providing a composition that inhibits the binding of p30 polypeptide of SEQ ID NO: 6 to the HVEM receptor wherein the composition is a soluble mouse HVEM:Fc chimeric protein; (4) a method for inhibiting a p30 polypeptide of SEQ ID NO: 6 mediated collagen induced arthritis in vivo comprising providing a composition that inhibits the binding of p30 polypeptide of SEQ ID NO: 6 to the HVEM receptor wherein the composition is a soluble mouse HVEM:Fc chimeric protein (page 56).

With the exception of the specific composition comprising the specific polypeptides mentioned above, there is insufficient written description about the structure associated with functions of *any* composition wherein the composition is any soluble p30 polypeptide, or *any* soluble HVEM polypeptide for the claimed method because there is no structure associated with the term "composition". Further, the term "modulates" in claim 31 can be stimulatory or inhibitory. There is insufficient written description about which autoimmune disease or T or B lymphoma or leukemia is stimulatory or inhibitory by the claimed method.

With regard to newly added claim 51, there is inadequate written description about the structure of any "fusion protein" because it is not clear what is being fused to the p30 polypeptide or the HVEM or LTβR. The specification discloses only chimeric protein comprising p30 polypeptide or the HVEM or LTβR fused to the Fc region of an immunoglobulin. With regard to

"functional fragment", there is inadequate written description about which fragment the specific amino acids within the full length of the p30 polypeptide or the HVEM or LTβR is functional.

With regard to newly added claim 52, the recitations of HSV gD-1, gD-1 (Δ290-299t) or LIGHT-t66 without SEQ ID NO have no structure such as amino acid sequence associated with function because said HSV gD-1, gD-1 (Δ290-299t) or LIGHT-t66 are merely a laboratory designation which does not clearly define the polypeptide in the claimed method, since different laboratories may use the same laboratory designations define completely distinct polypeptides.

Given the lack of a written description of *any* additional representative species of fusion protein, functional fragment of any p30 polypeptide, HVEM, LTβR for a composition used in the claimed method, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 9/16/02, 9/17/02 and 12/05/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) the claims have been amended. (2) The specification discloses four species having the requisite function, soluble HSV gD-1, gD-1 (Δ290-299t), HVEM:Fc, LTβR:Fc and LIGHT-t66 or any other composition that will have a structure that: 1) binds to a p30 polypeptide, HVEM or LTβR; and 2) inhibits binding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR.

In response to Applicant's argument, claims 26-32 still recite a method of inhibiting a p30 polypeptide-mediated cellular response using *any* composition. Given the indefinite number of composition, there is inadequately written description about the composition for the claimed method, let alone the structure of any polypeptide, antibody, DNA, or small molecule that: 1) binds to a p30 polypeptide, HVEM or LTβR; and 2) inhibits binding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR. Other than specific composition comprising the specific polypeptides mentioned above, there is insufficient written description about the structure of any composition that will have a structure that: 1) binds to a p30

polypeptide, HVEM or LTβR; and 2) inhibits binding of a cell surface expressed p30 polypeptide to a cell surface expressed HVEM or LTβR.

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

14. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
February 24, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600